Disease-modifying drugs for Multiple Sclerosis

Key Questions and Inclusion Criteria

Key Questions

1. What is the comparative effectiveness of disease-modifying treatments for multiple sclerosis, including use of differing routes and schedules of administration?

2. What is the effectiveness of disease-modifying treatments for patients with a clinically isolated syndrome?

3. What is the comparative tolerability and safety of disease-modifying treatments for multiple sclerosis?

4. Are there subgroups of patients based on demographics (age, racial or ethnic groups, and gender), other medications, or co-morbidities for which one disease-modifying treatment is more effective or associated with fewer adverse events?

Inclusion Criteria

Population(s)

Adult outpatients with Multiple Sclerosis[1, 2]:

Primary Progressive MS (PPMS)
Secondary Progressive MS (SPMS)
Relapsing Remitting MS (RRMS)
Progressive Relapsing MS (PRMS)

Adult outpatients with a clinically isolated syndrome (also known as 'first demyelinating event', first clinical attack suggestive of MS, or monosymptomatic presentation)[1]

Interventions (all formulations)

Glatiramer acetate (Copaxone®)
Interferon beta-1a (Avonex®, Rebif®)
Interferon beta-1b (Betaseron®)
Mitoxantrone (Novantrone®)
Natalizumab (Tysabri®)

Effectiveness outcomes

Multiple Sclerosis

- Disability
- Clinical exacerbation/relapse
- Quality of life

Clinically isolated syndrome

- Disability
- Clinical exacerbation/relapse
- Quality of life

- Functional outcomes (e.g., wheel-chair use, time lost from work)
- Persistence (discontinuation rates)

- Functional outcomes (e.g., wheel-chair use, time lost from work)
- Persistence (discontinuation rates)
- Progression to MS diagnosis

Safety outcomes

Overall rate of adverse effects
Withdrawals due to adverse effects
Serious adverse events
Specific adverse events (cardiovascular, hepatotoxicity, progressive multifocal leukoencephalopathy (PML), secondary cancers, etc.)

Other Outcomes

Interferon beta neutralizing antibodies
Rates of occurrence
Persistence with continued use
Impact on clinical outcomes (above)

Study designs

1. For effectiveness, controlled clinical trials and good-quality systematic reviews. Observational studies with two concurrent arms of at least 100 patients each and duration ≥1 year will be included (e.g. cohort, case-control).
2. For safety, in addition to controlled clinical trials, observational studies will be included.

References

1. McDonald WI, Compston A, Edan G, et al. Recommended diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the diagnosis of multiple sclerosis. *Annals of Neurology.* Jul 2001;50(1):121-127.

2. Poser CM, Paty DW, Scheinberg L, et al. New diagnostic criteria for multiple sclerosis: guidelines for research protocols. *Annals of Neurology.* Mar 1983;13(3):227-231.